REMARKS

Claim 19 has been amended in order to remove the limitation for the treatment of appetency disorders.

Claims 1-18 and 34-38, which are directed to the subject matter which was elected for prosecution and allowed in U.S. application Serial No. 09/341,765, were canceled in the preliminary amendment filed on January 11, 2002. Claims 30-33, being drawn to non-elected subject matter, were cancelled in the amendment filed on December 1, 2003. Claims 19-29 and 39 remain in the application.

Claims 19-23, 26-29 and 39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Barth et al. (U.S. Patent No. 5,624,941) and Baroni et al. (U.S. Patent No. 5,488,151) based on the following grounds cited by the examiner in the Office Action mailed on June 13, 2003:

> Barth et al. teach Applicants active agent, CB_1 receptor antagonist set forth in claims 19, 21 and 39 useful for the treatment of glaucoma. (abstract column 2, column 88, claim 27). Barth et al. also teach the dosage range of the CB1 receptor antagonist within the Applicants' range set forth in claims 27-29. (column 27, lines 10-35).
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> Baroni et al. teach Applicants active agent β3 agonist set forth in claims 19, 23 and 26 useful for the treatment of glaucoma. (abstract, columns 1 and 2, column 2, lines 32-35, column 4, claim 1). Baroni et al. also teach the dosage range of the β3 agonist within the Applicants' range set forth in claims 27-29. (column 3, line 63-column 4, line 11).
>
> The claims differ from the cited references in claiming combination of CB1 receptor antagonist, and β_3 agonist, to treat glaucoma. To employ combinations of CB1 receptor antagonist and β_3 agonist to treat glaucoma would have been obvious because all the components are well known individually for treating glaucoma. It would be expected that the combination of components would treat glaucoma as well. The motivation for combining the components flows from their individually known common utility (see *In re Kerkhoven,* 205 USPQ 1069(CCPPA 1980)). Therefore, it would have been prima

facie obvious to combine CB1 receptor antagonist, and β_3 agonist composition cojointly in a formulation to treat glaucoma.

This rejection is traversed and reconsideration and withdrawal thereof is respectfully requested for the reasons given hereinbelow.

Barth et al. (US Patent 5,624,941) disclose pyrazole derivatives having an affinity for cannabinoid receptors and are taught to be useful as immunomodulators and psychotropic agents, in thymic disorders, vomiting, myorelaxation, various types of neuropathy, memory disorders, dyskinesia, migraine, asthma, epilepsy and glaucoma or else in anticancer chemotherapy, in ischemia and angor, in orthostatic hypertension and in cardiac insufficiency. There is no disclosure anywhere in the cited patent of a pharmaceutical composition containing a combination of a pyrazole derivative having cannabinoid receptor affinity and any other active agent, let alone a regulator of metabolic functions or specifically a β_3 agonist. The second reference, Baroni et al. (US Patent No. 5, 488,151), discloses certain tetrahydronaphthalene compounds which act as β_3-adrenergic agonists. Baroni et al. suggest that it may be possible to use these compounds in the treatment of eye complaints, especially for the control of intraocular pressure and the treatment of ocular hypertension and glaucoma. The pharmaceutical compositions provided therein for the treatment of eye complaints, e.g. ocular hypertension and glaucoma, are ophthalmic formulations for topical administration to the eye; these formulations contain from 0.00001 to 1% by weight of the active β_3 agonists. Again, there is no suggestion that the β_3 agonists described therein can be used in combination with any other active agent, let alone with agents having affinity for cannabinoid receptors. Therefore, neither reference provides the requisite motivation to the person of ordinary skill to modify and combine the teachings of the cited references in order to arrive at the compositions of applicants' claims.

The Examiner has cited *In re Kerkhoven* for its holding that it is *prima facie* obvious to combine two compositions, each of which is taught to be useful for the same purpose...the motivation for combining the components flows from their individually known common utility. This statement is, nonetheless, only a partial reading of the cited case. The *In re Kerkhoven* opinion clearly states that "[i]t is prima facie obvious to combine two

compositions each of which is taught by the prior art to be useful for the same purpose, *in order to form a third composition which is to be used for the very same purpose*." (emphasis added). At most, Barth et al. and Baroni et al. may have suggested the use of the individually disclosed compounds in the treatment of numerous diseases, including glaucoma. However, the instantly claimed compositions are not taught to be useful for the treatment of glaucoma, but for the treatment of appetency disorders. Since two prior art compositions taught to be useful for perhaps the same purpose have not been combined to form a third composition which is to be used for the same purpose, Applicants believe the reasoning of *Kerkhoven* is not suitably applied in the context of the present circumstances.

Therefore, the claims are unobvious because there is no suggestion to combine the particular teachings in the prior art so as to obtain the invention claimed as a whole, and, hence, the 35 U.S.C. §103(a) rejection of claims 19-23, 26-29 and 39 based on said references is believed to be unwarranted and should be withdrawn.

Claims 19-22, 24 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Barth et al. (U.S. Patent No. 5,624,941) and Brazzell et al. (U.S. Patent No. 5,578,638) based on the following grounds cited by the examiner in the Office Action mailed on June 13, 2003:

> Barth et al. teach Applicants active agent, CB_1 receptor antagonist set forth in claims 19 and 21 useful for the treatment of glaucoma. (abstract, column 2, column 88, claims 27).
>
> Brazzell et al. teach β_3 agonist (formula IV) useful for the treatment of glaucoma. (abstract, column 1, lines 7-15, columns 3-7).
>
> The claims differ from the cited references in claiming combination of CB1 receptor antagonist, and β_3 agonist, to treat glaucoma. To employ combinations of CB1 receptor antagonist and β_3 agonist to treat glaucoma would have been obvious because all the components are well know individually for treating glaucoma. It would be expected that the combination of components would treat glaucoma as well. The motivation for combining the components flows from their individually known common utility (see *In re Kerkhoven*, 205 USPQ 1069(CCPPA 1980)). Therefore, it would have been prima facie

obvious to combine CB1 receptor antagonist, and β_3 agonist composition cojointly in a formulation to treat glaucoma.

This rejection is traversed and reconsideration and withdrawal thereof is respectfully requested for the reasons given hereinbelow.

Again, Barth et al. (US Patent 5,624,941) disclose pyrazole derivatives having an affinity for cannabinoid receptors and are taught to be useful as immunomodulators and psychotropic agents, in thymic disorders, vomiting, myorelaxation, various types of neuropathy, memory disorders, dyskinesia, migraine, asthma, epilepsy and glaucoma or else in anticancer chemotherapy, in ischemia and angor, in orthostatic hypertension and in cardiac insufficiency. There is no disclosure anywhere in the cited patent of a pharmaceutical composition containing a combination of a pyrazole derivative having cannabinoid receptor affinity and any other active agent, let alone a regulator of metabolic functions or specifically a β_3 agonist. The second reference applied, Brazzell et al. (US Patent No. 5,578,638), discloses multiple series of β_3 agonists, which are taught to be useful in the treatment of glaucoma and interocular hypertension. Brazzell et al. teach the use of the β_3 agonists alone, or in combination with other mechanistically distinct interocular pressure lowering ingredients such as β-adrenergic blocking agents, (e.g. timolol), carbonic anhydrase inhibitors, miotic agents (e.g. pilocarpine), epinephrine and dipivalylepinephrine, α_2 adrenergic agonists, prostaglandins or prostaglandin analogs. However, Brazzell et al. do not teach or suggest the combination of a β_3 agonist with any ingredients having affinity for cannabinoid receptors, as required by the instant claims. Therefore, there clearly is no motivation or suggestion to the person of ordinary skill to modify and combine the teachings of the cited references in order to arrive at the compositions of applicants' claims.

The Examiner has once more relied on *In re Kerkhoven*, in an attempt to establish a prima facie case of obviousness, but again the reasoning of *In re Kerkhoven* is not correctly applied in the instant case. The *In re Kerkhoven* opinion clearly states that "[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for

the same purpose, *in order to form a third composition which is to be used for the very same purpose*" (emphasis added). The cited references, Barth et al. and Brazzell et al. conceivably may have suggested the use of the individually disclosed compounds in the treatment of numerous diseases, including glaucoma. However, the instantly claimed compositions are not taught to be useful for the treatment of glaucoma, but for the treatment of appetency disorders. Since two prior art compositions taught to be useful for the same purpose have not been combined to form a third composition which is to be used for the same purpose, Applicants believe the reasoning of *Kerkhoven* is not suitably applied in the context of the present circumstances. Therefore, the claims are unobvious because there is no suggestion to combine the particular teachings in the prior art so as to obtain the invention claimed as a whole, and, hence, the 35 U.S.C. §103(a) rejection of claims 19-22, 24 and 25 based on said references is believed to be unwarranted and should be withdrawn.

Claims 19-22 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Barth et al. (U.S. Patent No. 5,624,941) and Cecchi et al. (U.S. Patent No. 5,130,339) based on the following grounds cited by the examiner in the Office Action mailed on June 13, 2003:

> Barth et al. teach Applicants active agent, CB_1 receptor antagonist set forth in claims 19 and 21 useful for the treatment of glaucoma. (abstract, column 2, column 88, claims 27).
>
> Cecchi et al. teach β_3 agonist (formula V) useful for the treatment of glaucoma. (Abstract, column 1, lines 38-column 2, line 21, column 17, lines 4-12).
>
> The claims differ from the cited references in claiming combination of CB1 receptor antagonist, and β_3 agonist, to treat glaucoma. To employ combinations of CB1 receptor antagonist and β_3 agonist to treat glaucoma would have been obvious because all the components are well know individually for treating glaucoma. It would be expected that the combination of components would treat glaucoma as well. The motivation for combining the components flows from their individually known common utility (see *In re Kerkhoven*, 205 USPQ 1069(CCPPA 1980)). Therefore, it would have been prima facie

obvious to combine CB1 receptor antagonist, and β_3 agonist composition cojointly in a formulation to treat glaucoma.

Barth et al. (US Patent 5,624,941) disclose pyrazole derivatives having an affinity for cannabinoid receptors and are taught to be useful as immunomodulators and psychotropic agents, in thymic disorders, vomiting, myorelaxation, various types of neuropathy, memory disorders, dyskinesia, migraine, asthma, epilepsy and glaucoma or else in anticancer chemotherapy, in ischemia and angor, in orthostatic hypertension and in cardiac insufficiency. There is no disclosure anywhere in the cited patent of a pharmaceutical composition containing a combination of a pyrazole derivative having cannabinoid receptor affinity and any other active agent, let alone a regulator of metabolic functions or specifically a β_3 agonist. The second reference cited for the instant rejection, Cecchi et al. (U.S. Patent No. 5,130,339), describes ophthalmic compositions of phenylethanolaminomethyltetralin compounds to be administered topically to the eye. These compositions are said to be useful for reducing interocular pressure, and as such, can be used in the treatment of ocular hypertension and glaucoma. The unit dosages, or eye drops, provided contain from 10 ng to 1 mg of the active compound, and can contain additional active principles, including antibiotics, anesthetics, steroid or corticosteroid anti-inflammatory agents which are suited for the treatment of glaucoma, but provoke as a side effect an increase in ocular pressure, or other high ocular pressure lowering agents. However, Cecchi et al. do not teach or suggest the combination of a β_3 agonist with any ingredients having affinity for cannabinoid receptors, as required by the instant claims. Therefore, there clearly is no motivation or suggestion to the person of ordinary skill to modify and combine the teachings of the cited references in order to arrive at the compositions of applicants' claims.

The Examiner has once again relied on *In re Kerkhoven* in an attempt to establish a prima facie case of obviousness, but again the reasoning of *In re Kerkhoven* is not correctly applied in the instant case. The *In re Kerkhoven* opinion clearly states that "[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same

purpose, *in order to form a third composition which is to be used for the very same purpose*." (emphasis added). The cited references, Barth et al. and Cecchi et al. conceivably may have suggested the use of the individually disclosed compounds in the treatment of numerous diseases, including glaucoma. However, the instantly claimed compositions are not taught to be useful for the treatment of glaucoma, but for the treatment of appetency disorders. Since two prior art compositions taught to be useful for the same purpose have not been combined to form a third composition which is to be used for the same purpose, Applicants believe the reasoning of *Kerkhoven* is not suitably applied in the context of the present circumstances. Therefore, the claims are unobvious because there is no suggestion to combine the particular teachings in the prior art so as to obtain the invention claimed as a whole, and, hence, the 35 U.S.C. §103(a) rejection of claims 19-22 and 25 based on said references is believed to be unwarranted and should be withdrawn.

In view of the foregoing amendments and remarks, reconsideration and withdrawal of the rejection of (a) claims 19-23, 26-29 and 39 under 35 U.S.C. §103(a), (b) claims 19-22 and 24-25 under 35 U.S.C. §103(a) and (c) claims 19-22 and 25 under 35 U.S.C. §103(a), is requested and allowance of claims 19-29 and 39 is respectfully requested.

Respectfully submitted,

Date: August 5, 2004

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